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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/554,533	BEELEY ET AL.	
	Examiner	Art Unit	
	Samuel W. Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/27/06 & 4/30/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-75* is/are pending in the application.

4a) Of the above claim(s) *63-65,72 and 73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55-62, 66-71 and 74-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/30/02*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *7/5/06*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 55-75 are pending.

The amendment filed 4/27/06 which cancels claims 1-54, and adds claims 55-75 has been entered. The applicants' request (filed 4/3/06) for extension of time of 3 months also has been entered.

Election/restriction

Applicants' election (filed 4/30/06) of Group II for examination without traverse is acknowledged wherein Applicants particularly elect the peptide of SEQ ID NO:29 for the examination. Yet, the election does not indicate which claims are in the elected Group II. The restriction requirement mailed 10/3/05 indicates that Group II includes claims 2-22 which have been canceled by the amendment filed 4/27/06. In communication with James Butler on July 5, 2006, Applicants were informed that claims 55-62 and 66-75 are drawn to the elected invention because claims 55-62 read on SEQ ID NO:29, claims 66-69 are obvious variation of the instant SEQ ID NO:29 which has Trp at residue 25 compared to Phe at residue 25 in SEQ ID NO:29, and process claims 70-71 and 74-75 which are directed to method of using the product of claims 55-62 and 66-69 are considered to be drawn into the elected invention. Claims 63-65, which are directed to patentably distinct peptide which amino acid sequence is distinct/different from SEQ ID NO:29, are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. The process claims 72-73 which depend form claim 63 are thus also withdrawn from further consideration.

Thus, Claims 55-62, 66-71 and 74-75 are examined in this Office action.

IDS

The references cited in the IDS filed 12/30/02 have been considered by the examiner.

Specification/Claim/ Objections

The disclosure is objected to because of the following informalities:

(1) On page 1, line 3 from the bottom, "SEQ. ID. NO. 1" should be changed to "SEQ ID NO:1"; and on page 11, line 15, "SEQ. ID. NOS. 67-74" should be changed to "SEQ ID NOs. 67-74". The similar changes should be made throughout the specification.

(2) The specification should clarify "PCT Application Serial No. ____" shown on page 4, lines 3-4 from the bottom.

(3) On page 14, line 15, "Figure 4 depicts" should be changed to "Figures 4A-4B depict".

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 55-62, 66-71 and 74-75 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 55 and 66 and dependent claims thereof, as written, do not sufficiently distinguish over other peptide or polypeptide or protein, as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor. See MPEP 2105.

Claim Rejections - 35 USC § 112, the second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 56, 58, 61, 67-68, 70-71 and 74-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 56, 58 and 61 set forth "Xaa_2 is Ser", "Xaa_3 is Asp" and "Xaa_{28} is Ala", respectively, which do not read on the elected SEQ ID NO:29 peptide sequence. These claim limitations are drawn to non-elected subjected matter, which render the claim indefinite. Similarly, see also claims 67 and 68.

Claims 70 and 74 indefinite because the claimed method lacks the subject to be administered. The dependent claims are also rejected.

Claim 71 recites "*administration of a therapeutically effective amount of an insulin*"; the recitation is not apparent whether or not the insulin is co-administered or/and separately administered with the peptide compound of claim 55.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 55-62, 66-69, 70-71 and 74-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the

art may be found not to have been placed in possession of a genus...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163 does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

In the instant case, the claims are drawn to a method of increasing the efficiency of an intein-mediated protein splicing/ligation comprising expressing a fusion protein comprising said intein.

(1) Physical and/or chemical properties:

The current claims 55 and 66 and the dependent claims thereto do not describe biological function of the claim protein. The instant invention has not been described in such a way that it is clear that the applicant invented what is claimed. Without knowing the assayable biological function of the claimed peptide, the skilled artisan will not know how to characterize and use the claimed peptide, e.g., for treating diabetes mellitus disorder. Since the written description must therefore communicate that which is necessary to enable the skilled artisan to make and use the functional peptide claimed, the current invention needs to fulfill the written description requirement stated above.

(2) Functional characteristics:

Without knowing the biological function of the claimed peptide, one skilled in the art are unable to assay or characterize functional peptide in order to treat a disorder state, e.g., diabetes mellitus.

(3) Level of skill and knowledge in the art:

The general knowledge and level of skill in the art do not supplement the omitted description with respect to the biological function/activity of the claimed peptide. When the claimed peptide is chemically synthesized (Example 29, pages 49-50), the functional parameter is required for one skilled in the art to be able to assay and characterize the synthesized exendin

agonist peptides, which may not be homogenous due to chemical (covalent or non-covalent) modification(s) to amino acid residue(s) of the synthesized peptides thereof.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 55, 57, 59-60, 62, 66 and 69 are rejected under 35 U.S.C. 102(e) as being anticipated by Young et al. US Pat. No. 6858576 B1).

In Example 31, Young et al. teach an exendin agonist peptide having SEQ ID NO:32 which has 100% sequence identity to the instant SEQ ID NO:29, wherein SEQ ID NO:29 reads on the peptide sequence set forth in claim 55, and wherein residues 2, 3, 8, 10, 14, 22, 23 25 and 28 are Gly, Glu, Ser, Leu, Leu, Leu, Phe, Phe and Asn, respectively. The Young et al. teaching anticipates instant claims 55, 57, 59 and 60.

On columns 45-46, Young et al. teach that the SEQID NO:32 peptide contains amidated Ser at carboxyl terminus, which anticipates instant claim 62.

In Example 5, Young et al. teach an exendin agonist peptide having SEQ ID NO:6 which has 100% sequence identity to the peptide set forth in claim 66, wherein residues 2 and 3 are Gly and Glu, respectively. The Young et al. teaching anticipates instant claim 66.

On columns 27-28, Young et al. teach that the SEQID NO:6 peptide contains amidated serine residue at carboxyl terminus, which anticipates instant claim 69.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 55, 57, 59-60, 62, 66, 69-71 and 74-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. US Pat. No. 6858576 B1).

The rejection to claims 55, 57, 59-60, 62, 66 and 69 has been discussed above.

Young et al. doe not set forth working example or claim the method of treating a diabetes state comprising administering to a subject the above-mentioned exendin agonist peptide.

On column 3, however, Young et al. teach that the exendin agonist peptide is useful for treating post-prandial hyperglycemia, a complication associated with type 1 (insulin dependent) and type 2 (non-insulin dependent) diabetes mellitus. When administered, the exendin agonist will inherently treat the diabetic disorder, as applied to instant claims 70-71 and 74-75.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to develop the method of treating diabetes mellitus in a subject comprising administering to said subject the exendin ageist peptide (e.g., SEQ ID NO:29). One skilled in the art would have been motivated to do this because Young et al. have taught usefulness of the exendin agonist peptides in treatment of the diabetes, and because Young et al. have also taught formulation of the exendin agonist peptide into a pharmaceutical composition and administration route for the composition thereof (see columns 13-14).

Therefore, the claimed invention was *prima facie* obvious to make and use the invention at the time it was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Weber, Jon, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Samuel Wei Liu, Ph.D.
Art Unit 1653, Examiner
July 5, 2006

Jon Weber
Supervisory Patent Examiner